

EXHIBIT C



A plasma only integrated somatic and epigenomic circulating tumor DNA (ctDNA) assay to inform recurrence risk in colorectal cancer (CRC).

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Abstract #3602

Introduction

- ctDNA has been shown to identify patients at high risk for disease recurrence post CRC resection
- Current ctDNA residual disease detection approaches only assess genomic alterations (alts), are limited by low levels of ctDNA, and rely on tumor tissue sequencing to differentiate tumor derived alts from confounding non-tumor derived alts (e.g. clonal hematopoiesis of indeterminate potential; CHIP)
- We evaluated a plasma only ctDNA assay which assesses genomic and epigenomic signals to identify CRC pts at high risk of recurrence without requiring initial tumor tissue sequencing

Methods

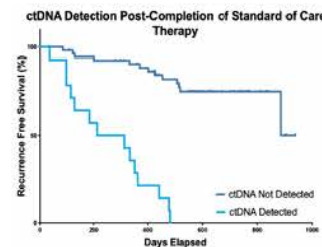
- 72 patients with CRC underwent standard of care (SOC) treatment for CRC which included surgery +/- neoadjuvant therapy (N = 42), or surgery and adjuvant therapy +/- neoadjuvant therapy (N = 30) and had a post-completion of SOC therapy plasma sample collected (3-4mL of plasma)
- Extracted ctDNA (median 27ng) was analyzed using a single plasma sample NGS test validated in early stage CRC that integrates assessment of genomic alts with epigenomic cancer signature. A variant classifier differentiates tumor derived from non-tumor derived alts (e.g. germline or CHIP alts) in a tumor tissue uninformed approach (LUNAR assay, Guardant Health, CA. Figure 1; See Abstract #3057 for assay analytical validation)
- Post-completion of SOC therapy plasma samples were collected a median of 31 days after surgical resection (N = 42) or a median of 37 days after adjuvant therapy completion (N = 27)
- Median follow-up is 515 days (33 – 938 days)

Cohort Demographics		Number of patients	(%)
Gender	Male	48	67%
	Female	24	33%
Median Age at diagnosis (range)	61 years (31 – 84 years)		
Stage (at resection)	0 - II	27	38%
	III	21	29%
	IV	24	33%



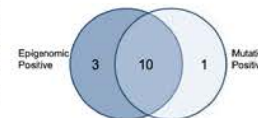
Figure 1: Overview of the LUNAR assay which integrates a digital genomic sequencing with quantification of cancer associated epigenomic signals for a ctDNA detected / not detected result

ctDNA detection after completion of standard of care therapy had a recurrence positive predictive value (PPV) of 100%, negative predictive value (NPV) of 76%, and a hazard ratio for recurrence of 9.22 ($p < 0.0001$).



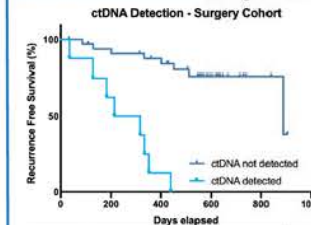
Assay Performance by Analysis		
	Genomic (N)	Integrated Genomic and Epigenomic (N)
PPV (N of patients with ctDNA detected who recurred)	100% (11 / 11)	100% (14 / 14)
NPV (N of patients with ctDNA not detected who were recurrence free)	72% (42 / 58)	76% (42 / 55)
Sensitivity for recurrence within one year of surgery	56% (9 / 16)	69% (11 / 16)
Specificity for recurrence within one year of surgery	96% (51 / 53)	94% (50 / 53)

Cohort results by genomic sequencing versus epigenomic analysis. Of the 14 patients who were ctDNA positive after completion of SOC therapy, 10 were positive for both by genomic and epigenomic assessment.



Results

In the **surgery cohort**, ctDNA detection had a recurrence PPV of 100%, NPV of 76%, and a hazard ratio for recurrence of 8.7 ($p < 0.0001$).

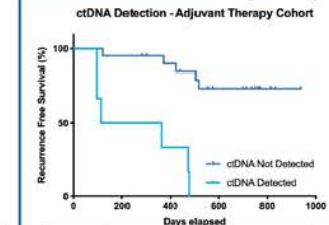


	Recurrence	Recurrence-free	Total
ctDNA +	8	0	8
ctDNA -	8	26	34
Total	16	26	42

Sensitivity and Specificity of ctDNA for recurrence within one year:

Sensitivity	64%	7 / 11 patients with a recurrence at 1 year following surgery were ctDNA detected post CRC resection
Specificity	97%	30 / 31 patients who were recurrence-free at 1 year following surgery were ctDNA not detected post CRC resection

In the **adjuvant therapy cohort**, ctDNA detection had a recurrence PPV of 100%, NPV of 76%, and a hazard ratio for recurrence of 9.3 ($p < 0.0001$).



	Recurrence	Recurrence-free	Total
ctDNA +	6	0	6
ctDNA -	5	16	21
Total	11	16	27

Sensitivity and Specificity of ctDNA for recurrence within one year:

Sensitivity	80%	4 / 5 patients with a recurrence at 1 year following surgery were ctDNA detected post completion of SOC adjuvant therapy
Specificity	91%	20 / 22 patients who were recurrence-free at 1 year following surgery were ctDNA not detected post completion of SOC adjuvant therapy

Conclusions

- In resected CRC, ctDNA detection utilizing a plasma only, tumor uninformed integrated genomic and epigenomic assay has high recurrence PPV and NPV following completion of standard of care therapy
- In the post-resection setting, ctDNA detection identifies pts who may benefit from adjuvant therapy. Post completion of adjuvant therapy, ctDNA identifies pts who may benefit from additional/modified therapy
- These findings demonstrate that a single blood draw post-resection / post-adjuvant therapy, ctDNA can identify high risk pts and inform therapy decision making

References

- Oveman, et al. 2017. J Clin Oncol 35, 2017 (suppl; abstr 3522).
- Tie et al. 2018. J Clin Oncol 36, 2018 (suppl; abstr 3516)